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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,039	06/23/2005	Tetsuro Kokubo	4439-4023	8665

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
05/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,039	KOKUBO ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-8-04&7-11-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-20-07 has been entered.

Claims 2-9 have been canceled. Claims 1 and 10 remain pending and under consideration.

The amendment filed 12-28-06 should not be entered because it is defective - claims 1 and 10 are missing the marked up version of the "comparing..." step 5. To expedite prosecution, it is assumed the phrase has been deleted, and the amendment has been entered.

Applicant's arguments filed 12-28-06 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 10 encompass a method of monitoring expression of a gene in a human having a PHM4 gene knocked out which is non-statutory subject matter.

Claim Rejections - 35 USC § 112

New Matter

Claims 1 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support for the amendments to claims 1 and 10 has not been provided and cannot be found in the specification as originally filed.

In particular, the phrase animal or a yeast whose PHM4 gene is knocked out" cannot be found.

Claim 1 and 10 remain rejected under new matter for reasons of record as follows:

The phrase "target gene" in claims 1 and 10 is new matter. Support cannot be found in the claims or specification as originally filed. Applicants point to original claim 9, which has a smaller scope than now, claimed. Claim 9 was limited to monitoring a target gene of a transcription factor. Paragraph 18 of the published application is also limited to target genes of transcription factors.

The step of "preparing a plasmid in which a polyphosphate kinase (PPK) gene is connected in frame and downstream of the target gene" is new matter. Support cannot be found in the claims or specification as originally filed. Applicants point to paragraph 13 of the published application, which is limited to plasmids carrying PHM4 genes downstream of the GAL1 promoter. Likewise, paragraphs 16, 19 and 25 are much more limited than the phrase as written. Furthermore, paragraph 16 relates to polyphosphate synthetase not polyphosphate kinase (line 3). Paragraph 19 is limited to PPK operably linked downstream to a promoter of a chosen gene wherein expression is monitored by the amount of polyphosphate accumulated as determined by NMR. Paragraph 25 is limited to PHM4 downstream of the GAL1 promoter used to transform PHM4 knockout yeast cell lines.

The step of "introducing the plasmid into a host cell, a tissue or an organ" in step 2 of claims 1 and 10 is new matter. Support cannot be found in the claims or specification as originally filed. Applicants point to paragraph 25, which is limited to introducing a plasmid to PHM4 knockout yeast cell lines and selecting transformants using selective media.

The step of "inducing expression of the PPK gene" in step 3 of claims 1 and 10 is new matter. Support cannot be found in the claims or specification as originally filed. Paragraph 25 is limited to inducing expression of the PHM4 gene.

The step of quantifying in step 4 of claims 1 and 10 is new matter. Support cannot be found in the claims or specification as originally filed. Applicants argue support is found in paragraph 19 of the published application. Applicants' argument is

not persuasive. Paragraph 19, 20 and 25 are limited to monitoring expression of a chosen gene using a PPK gene placed downstream of a promoter of the chosen gene and quantifying the amount of polyphosphate by NMR.

Enablement

Enablement cannot be addressed at this time because the claims are so unclear. In particular, the combination of PHM4 knockout animals having a plasmid in which a PPK gene is "connected in-frame and downstream of the target gene" and "introducing the plasmid in to a host cell, tissue or organ and selecting a transformant, and culturing the transformant" does not clearly indicate the claims encompass in vivo embodiments. Accordingly, the examiner cannot properly analyze the claims for enablement.

Indefiniteness

Claims 1 and 10 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the host" in the preamble of claims 1 and 10 lacks antecedent basis.

Claims 1 and 10 require an animal or yeast in which the PHM4 gene is knocked out in the preamble, but the body of the claim requires a plasmid encoding PPK operably linked downstream of a target gene. The structure of the plasmid does not correlate to a knockout of PHM4. Accordingly, the structure of the animal or yeast is wholly unclear.

It is unclear how the "host" in the preamble relates to the "host cell, a tissue or an organ" in the body of the claim.

Claims 1 and 10 are indefinite because the phrase "quantifying accumulation of polyphosphate having a strand length equal to or less than 50 mer in the mean value and produced by the transformant after the expression has been induced" does not make sense. It appears that the phrase is intended to limit which polyphosphates are being quantified; however, the phrase does not clearly set forth the metes and bounds of the polyphosphates being quantified. It cannot be determined how to distinguish PPK made by the transformant after expression has been induced from PPK made by the transformant before expression is induced. It cannot be determined how to distinguish polyphosphates having a mean value strand length equal or less than 50 mer from those that do not.

Applicants point to paragraph 16 of the published application, which states:

> "Polyphosphate synthetase genes, for instance PHM genes of Saccharomyces cerevisiae, specifically PHM 1-4 genes placed downstream of the chosen gene and in-frame with it allow transcription to be quantified in real time. The polyphosphate generated by this method has a mean length of up to 50 phosphate groups, within the detectable range by NMR. The 10 mer is thought to show the highest sensitivity for 31P-NMR. The polymer sizes can be confirmed by staining the cell contents with toluidine blue after polyacrylamide gel-electrophoresis.

Applicants' argument is not persuasive. Quantifying the amount of polyphosphate generated having a mean length of up to 50 phosphate groups is not the same as the quantifying step claimed. Furthermore, it is unclear how a polyphosphate can have a mean length of 50 phosphate groups.

The metes and bounds of when NMR is "non-destructive" in claims 1 and 10 remain unclear. Applicants point to paragraphs 5 and 6 of the published application and an abstract from 2005. Applicants' arguments are not persuasive. Paragraphs 5 and 6

do not define the term. The abstract cannot establish the phrase was well known in the art at the time of filing because it was published in 2005, which is after the filing dates of the instant application.

The metes and bounds of "real time" remains unclear.

It is unclear how "performing one-dimensional ^{31}P-NMR measurement" correlates to "quantifying the accumulation of polyphosphate" in step 4 of claims 1 and 10. It is unclear if they are separate steps or if the "performing" further limits how the "quantifying" is performed.

The phrase "without adding an exogenous substrate" in step 4 of claims 1 and 10 is indefinite. The phrase appears to relate to how the expression of PPK is induced and not how PPK expression is quantified as claimed. Applicants argue the phrase distinguishes the invention from the prior art. Applicants' argument is not persuasive because the claim implies PPK expression is induces without adding an exogenous substrate and does not clearly state PPK expression is quantified without adding an exogenous substrate.

Claims 1 and 10 are unclear because they do not recite a step in which the results are interpreted. It cannot be determined how quantifying polyphosphate using NMR correlates to monitoring expression of a target gene.

Claim Rejections - 35 USC § 102

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by {Sharfstein (1994) Ann NY Acad. Sci. 745:77-91} has been withdrawn. Sharfstein taught transfecting bacteria with a plasmid encoding the polyphosphate operon, which

inherently has the PPK gene connected in frame and downstream from a target gene as claimed. Sharfstein did not teach monitoring expression of a target gene in a yeast or animal whose PHM4 gene is knocked out as claimed.

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by {van Voorthuysen (2000) J. Biotech. 77:65-80} has been withdrawn. van Voorthuysen did not teach monitoring expression of a target gene in a yeast or animal whose PHM4 gene is knocked out as claimed.

Conclusion

No claims allowed

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

Michael C. Wilson
Patent Examiner